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Evaluation of Patient Driven Digital Mole Monitoring

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1. Abstract

Introduction: The incidence of malignant melanoma is still rising. Besides high mortality, malignant melanoma causes a growing economic burden on many health care systems. Primary prevention measures already being widely accepted nowadays, the focus now lies on secondary prevention, especially on earlier detection. Not only are there new diagnostic possibilities for professionals, but also do patients get more and more involved in the diagnostic process. Smartphone applications allow patients to monitor their moles. However, so far there is little known about the impact of these applications and the feasibility of patient driven mole monitoring in general.

Methods: After an overview of the established diagnostics of melanoma and some relevant new approaches for professionals and patients, this paper contains a data collection part. In form of a feasibility study, a web-based survey taught participants about mole monitoring and then presented them cases of combined follow-up images. Participants were asked to evaluate whether or not a mole had changed significantly. The primary endpoint was defined to be the overall concordance of the assessments of patients with the ones of an expert dermatologist.

Results: 47 recruited volunteers and 19 participants with a dermatological background contributed 799 and 292 assessed images respectively. Looking at the overall concordance of patients completing the survey with the assessment of the expert dermatologist, a score of 80.42 % (confidence interval 76.912 – 83.922 %) was reached (mean = 24.13, standard deviation = 2.49, median = 24.00 (17.00 - 29.00)).

Conclusions: Many of the papers evaluating the new diagnostic tools conclude a great potential but criticise the often missing underlying evidence. As this paper shows, patient education for mole monitoring seems in a tendency feasible and also favoured by many patients. Against the backdrop of dwindling resources in many health care systems, self-monitoring might be a way for patients to take responsibility themselves. Although the participants in this paper did not reach the overall concordance of 90 % previously defined as significant, the result can be regarded as respectable. Thus, and because sample sizes are small, results can only be interpreted as tendencies and in a speculative manner. For a better significance and quantification of the impact of teaching as well as the feasibility of patient driven monitoring, more extensive studies should be conducted taking up our approach.

2. List of Abbreviations

NMSC	Nonmelanoma skin cancer
BCC	Basal cell carcinoma
SCC	Squamous cell carcinoma
UV	ultraviolet
SDDI	Sequential digital dermoscopy imaging
ST-SDDI	Short-term sequential digital dermoscopy imaging
LT-SDDI	Long-term sequential digital dermoscopy imaging
PCP	Primary care physician
RCM	Reflectance confocal microscopy
EIS	Electrical impedance spectroscopy

3. Introduction

3.1. Skin Cancer – Epidemiological Situation and Challenges

The incidences of skin cancer, both melanoma and nonmelanoma skin cancer (NMSC), are still rising. Nonmelanoma skin cancer includes basal cell carcinoma (BCC) as well as squamous cell carcinoma (SCC). In white populations throughout the world, the incidence rates of cutaneous melanoma even increase the most rapidly over all cancers.[1, 2] An estimated annual increase between 3 and 7 % suggests that the incidence is going to double every 10-20 years.[1] Switzerland being ranked third place in 2012, the two highest incidence rates in the world are found in Australia and New Zealand where they have gone up to 60/100'000 and where consequently, cutaneous melanoma is one of the most frequent cancer types of them all.[2, 3, 4] Understandably, this has a considerable impact on the economic burden of disease.

Melanomas develop from neural crest-derived melanocytes, pigmented cells that are usually located in the epidermis, and sometimes in the dermis.[5] Although some aspects of the aetiology of melanoma are still not completely understood or sufficiently quantified, the predominant environmental risk factor has been shown to be the exposure to ultraviolet (UV) radiation.[5, 6] Studies indicate that an intermittent form of sun exposure that leads to irregular but intense contact with UV radiation increases the risk of melanoma, whereas a steady or chronic exposure seems to be paradoxically inversely associated with melanoma.[6] In addition to familiar predisposition which contributes only approximately 5-10 % to the total number of melanoma cases, individual factors such as sex, skin type or sunburn play an essential role.[5] The fact that the association between melanoma and sunburn history has turned out to be stronger in studies including a higher percentage of fair-skinned controls confirms that there is also a geographical component when it comes to risk factors of melanoma. The reason for this is that the proportion of fair-skinned individuals in a population grows with increasing latitude.[5, 6] What is missing so far in the list of risk factors are the various life style parameters such as outdoor/indoor life, sunburn or vitamin D and antioxidant protection.[6] Amongst these life style factors, there are several that underwent change in our society simultaneously with the beginning and still ongoing increase of melanoma incidence, for instance when it comes to the habits in

leisure activity or places of work (indoor and outdoor). That is where the primary prevention begins. Cautious sun exposure is regarded as the most straightforward measure to protect from skin damage and includes avoidance of the midday's sun, solarium visits, the use of adequate clothing, sunhats and sunglasses and appropriate sunscreen agents.[7] Apparently, these recommendations were not even enough to slow down the increase of incidence rates of melanoma. However, the acceptance of sun exposure as a danger came up after a general unawareness of this correlation before 1990.[6]

In contrast, secondary melanoma prevention aims at detecting an already developing melanoma as early as possible. New technologies with auspicious approaches are deployed when it comes to the detection of melanoma. However, it needs to be considered that the increase in melanoma incidence cannot merely be led back to better methods in recording data or to changes in diagnostic criteria.[8] While some studies propose a stabilization or even decrease of mortality rates from cutaneous melanoma as a consequence of earlier detection,[1, 9] a recent analysis in the US showed that the incidence of invasive melanoma increases on a lower level than the mortality rate which means that we might not yet see the efforts of an earlier detection.[10]

Nevertheless, it should be emphasised that the incidences of melanoma in situ and thinner invasive melanoma increase faster than that of thicker invasive melanoma, which can be interpreted as a benefit of earlier detection.[2, 9, 10]

In an Italian study, 40.6 % of enrolled melanoma patients recognized the lesion as being suspicious of melanoma themselves, in 12.5 % of the cases it was their spouse. This underlines why melanoma early diagnosis strategies, which secondary melanoma prevention is aiming at, should absolutely include the patients themselves with their ability to detect change of a mole. Moreover, it emphasises the role of skin self-examination and mole monitoring.[11]

3.2. Development in Diagnostics

Dermatologists with a certain amount of experience can diagnose most of the melanocytic lesions with the unaided eye.[12] In uncertain cases they often use dermoscopy in addition but nonetheless, even in combination there is still no diagnostic accuracy of 100 %. To be sure, histopathological examination is needed which remains the gold standard in the diagnosis. However, in patients with multiple and many sus-

picious melanocytic lesions it is somewhat impractical to excise all of the lesions to have them examined by the histopathologist.[12] In order to prevent benign lesions from being excised and to detect changes that indicate malignancy, dermatoscopic monitoring is being used. This technique enables a detailed view of subsurface structures and furthermore a comparison over time. This technique is supposed to help diagnose melanoma early since change is a highly sensitive marker for melanoma.[13] Until some years ago, devices for digital dermoscopic monitoring had been reserved for professionals. However, attachments to smart phones have become available recently as well as applications that take and afterwards store pictures of moles even without attachments using different technical approaches (see chapter 5.3). Thus, it might only be a question of time until patients will extensively start using these new possibilities.

Although different aspects of the melanoma development still remain unclear, it is widely believed that varying degrees of dysplasia precede the process of malignant transformation in the tumour entity melanoma as well. Nevertheless, in the majority of melanomas there is no evidence or no clear anamnesis of a pre-existing melanocytic nevus at the later melanoma site.[14] The percentage of the melanocytic nevus component lies between 10.8 % and 57.6 % according to the data published in scientific literature.[14] Surprisingly, amongst the pre-stages before malignant transformation, the dysplastic nevus has not been found most often. Dermal and congenital nevi have been reported as being the most prevalent types.[14] An other recent study from Turkey states that most melanomas develop de novo.[15]

Breaking this down to the diagnostic process, this means that melanoma can be discovered either as a newly evolving lesion or as a changing lesion that already existed before as a form of a melanocytic nevus. If a lesion appears out of nothing, it may lead the patient to a doctor sooner or later or directly to a dermatologist, but if a pre-existing lesion undergoes change that has to be noticed first. Either dermatologists detect it during a routine skin control or in the context of a screening programme or the patients themselves notice the change. When it comes to secondary melanoma prevention, patients at risk are controlled more often nowadays. And to make it more likely that patients detect change of a lesion on their own, there are devices and smart phone applications coming on the market. They are supposed to help patients observing moles or assessing moles they consider suspicious somehow. In an Italian study, 40.6 % of melanomas have apparently already been detected by the patients

themselves, presumably without any further technical support.[11] Thus, there seems to be enormous potential for a better and earlier detection thanks to these upcoming devices and possibilities. At the same time, physicians might increase their sensitivity in detecting changing moles and melanoma in general by introducing new and adjunct techniques in their routine work (see chapter 5.2). It would be highly gratifying if these developments finally succeeded in decreasing or at least stabilizing mortality rates of melanoma patients. However, in order for a new technique to be established, requirements must be met and it needs to be applied correctly.

3.3. Goals of the Project

In a first part, this project intends to give an overview of the current professional approaches in the detection of suspicious moles, established routines as well as the mentioned newly evolving techniques. Moreover, the project wants to discuss how patients themselves can contribute to an earlier detection, which is the main effort of secondary melanoma prevention.
In a second part, the paper discusses the results of a conducted survey evaluating aspects of the feasibility of mole monitoring by patients themselves.

Over the whole of the project, the following questions were addressed:

1) What is sequential digital dermoscopy imaging („monitoring“) exactly and what is its significance in skin cancer diagnostics for professionals and patients?

2) Are patients able to assess whether or not a lesion has changed significantly in short- or long-term monitoring when comparing follow-up and baseline pictures of the same lesion after an initial short tutorial explaining how to do so? Is digital follow-up feasible by patients themselves?

3) Is there a difference in the performance of participants who got feedback to each of their assessments in comparison to those who did not?

4) What is the patients' view on the subject?

4. Materials and Methods

4.1. Design

The paper is considered a feasibility study. It is a small research project using already existing health-related, anonymous and non-genetic data. The collection of new data for the study part of this paper has been conducted in form of a web-based survey to which recruited participants found access over an URL (uniform resource locator) or a QR-code (quick response code). For the theoretical part about the point of view and current development in diagnostics at the beginning of the paper, literature and publications found mainly on PubMed were considered as well as direct information, for instance in form of brochures and material from manufacturers themselves.

4.2. Setting

The data collection part of this paper is based on data gained through a survey which we created from scratch on the platform SurveyMonkey (SurveyMonkey Inc., San Mateo, California, USA, www.surveymonkey.com). It consisted of three major parts. After a short introduction informing the participant about the purpose and the idea behind the study and some statistical questions and superficial questions concerning their own mole history, there was first a tutorial. This tutorial contained relevant information about dermoscopy, its significance and the different types of mole monitoring, that is short-term sequential digital dermoscopy imaging (ST-SDDI) and long-term sequential digital dermoscopy imaging (LT-SDDI). Moreover, it was explained to the participants what “change” regarding moles means and which forms of change are considered to be significant and non-significant using the criteria Kittler and Menzies defined in 2005 (see chapter 5.1).[12] Then some examples with explanations followed for the participants to get familiar with the criteria (see illustrations 3-8 taken from the survey at the end of this subchapter). An “example” consisted of two sequential dermoscopy images of the same mole that had been aligned precisely next to each other and combined into one single image. The left side displayed the initial baseline picture whereas the right side displayed the follow-up picture of the lesion (see illustration 1). The pictures had been provided by a database in Sydney, Australia.

Second, a test set containing 10 of these examples followed, where the participants were supposed to practise and deepen their knowledge acquired in the preceding tutorial. They were always asked the same question, whether or not the mole shown has in their opinion changed significantly over the period of time between the baseline and the follow-up picture. Every answer was immediately registered via the online platform and they got a feedback whether their answer had been correct or not. After the completion of the test set, the participants were asked how familiar they felt so far with the assessment of moles in terms of change in accordance with the criteria studied in the tutorial and repeated in the test set. If they answered “familiar” or “rather familiar”, they were forwarded to the third part of the survey, which is the main survey. The main survey contained 30 examples that the participants had to assess in the same way as before in the test set. In case they answered “rather unfamiliar” or “unfamiliar”, they were asked whether they wanted to quickly go through tutorial and test set again in order to hopefully feel more familiar afterwards and then start the main survey or if they wanted to abandon without participating in the main survey and thereby without contributing data to the study.

Illustration 1: Example of a follow-up case presented to the participants

Although in clinical practice, the rate of significant changes in moles is only around 10 %, we included more cases with change in order to prevent the participants from getting bored and losing focus. We thereby tried to find a balance and to include enough events to keep the participants’ engagement high without presenting a ridiculous situation that would never occur. Bearing in mind that participants would probably not compare an endless number of images attentively, we thought of scheduling a total of 30 cases. Among these, 6 cases (= 20 %) showed an event in form of signifi-

cant change.

After the completion of the survey, the participants were conclusively asked whether or not they could at all imagine observing their own moles in the foreseeable future, for instance by using upcoming applications working with the technique of monitoring.

The participants completed different variants of the survey. In variant 1 they got feedback on whether or not their answer had been correct after assessing every example in the main survey, in variant 2 they did not get a feedback. In the test set they got feedback in both variants. Thereby, the influence of feedback on the performance of the participants was supposed to be evaluated in order to shed light on how the optimal preparation for self-monitoring should look like. The participants randomly took or got a flyer with a URL and a QR code leading directly to either variant 1 or variant 2 (see illustration 2 for the visualised logic circuit of the survey).

The participants with a dermatological background were led to a separate collector of the feedback version of the survey. Thereby, a maximal learning effect was supposed to be provided, mainly for younger colleagues who might not have a lot of experience in monitoring yet.

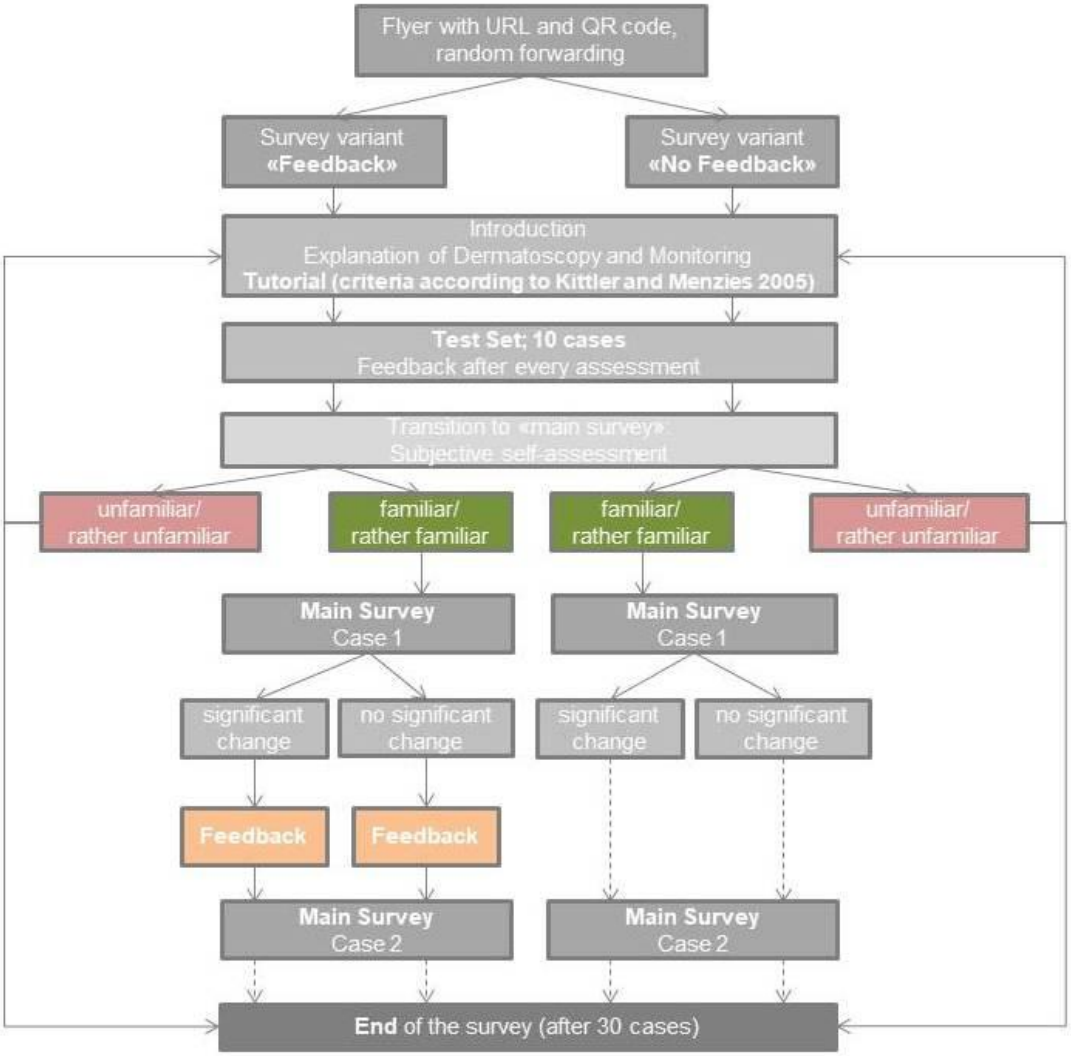
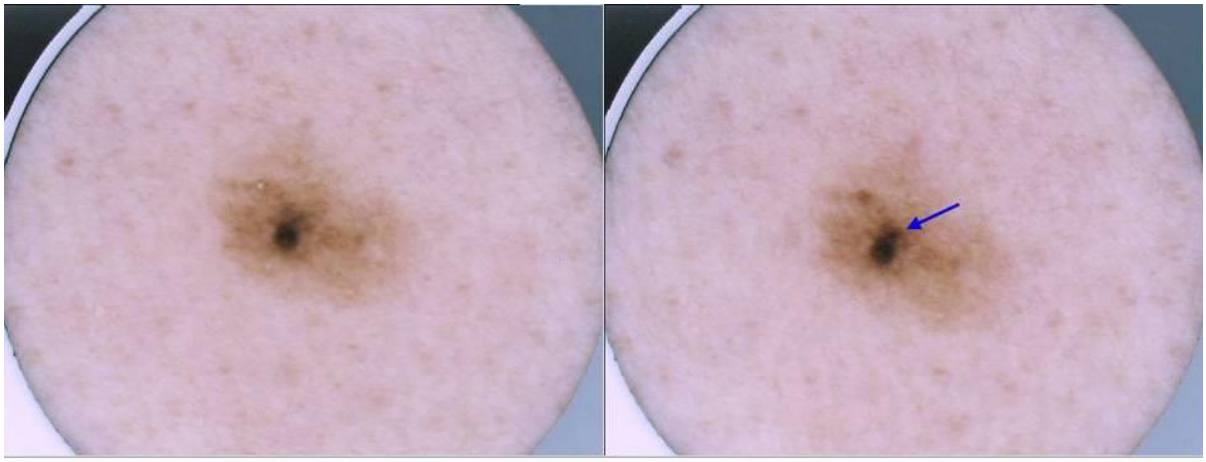


Illustration 2: Visualisation of the logic circuit of the survey

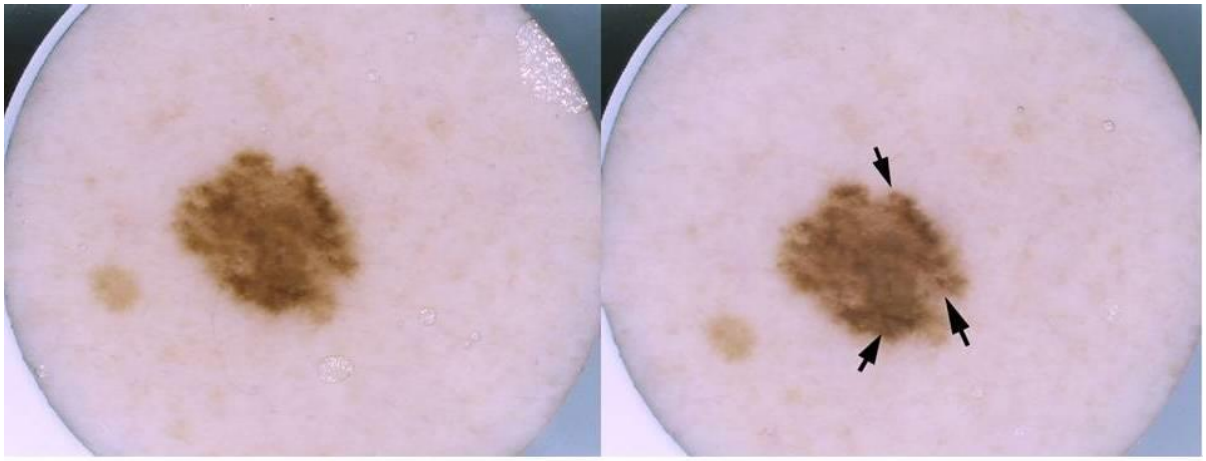


Tutorial (1): Im Verlauf (Follow-Up, rechts) ist eine Ausdehnung des dunkelbraunen Areals zu erkennen – der Pfeil zeigt einen dunklen Ausläufer.

Zwischen den beiden Aufnahmen liegen nur 6 Wochen. Bei der Kurzzeit Verlaufskontrolle **(Zeitraum: 3 Monate)** ist **jede Veränderung signifikant.**

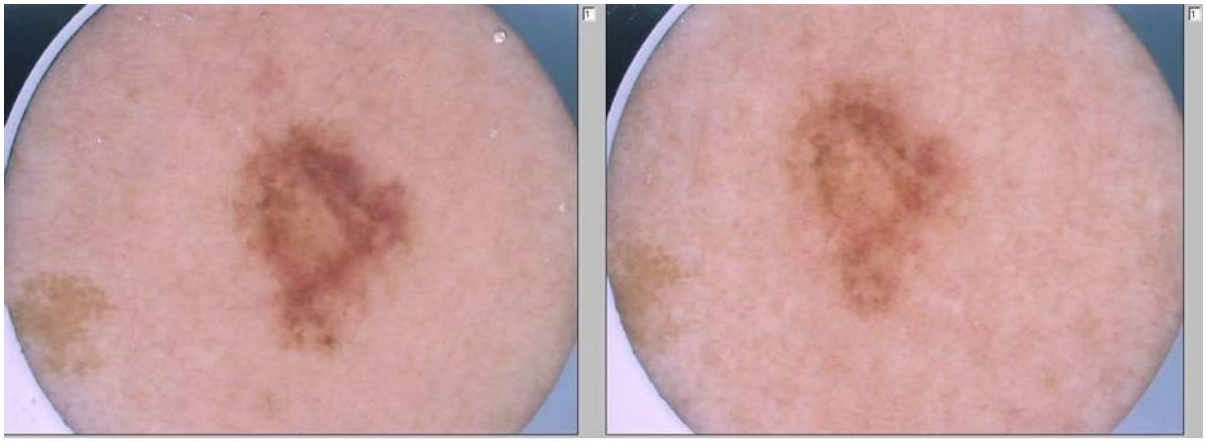
Zwei Ausnahmen:
1. Die gesamte Läsion ändert die Pigmentierung (ganzes Muttermal wird heller oder dunkler, z.B. Sonnenlicht-induziert zusammen mit der umliegenden Haut)
2. Verlust oder Neuauftreten von kleinen weisslichen Punkten (Zysten)

Illustration 3: Part of the tutorial, example 1 with comments (in German)



Tutorial (2): Im Verlauf (Follow-Up, rechts) sind bei ganz genauer Betrachtung mehrere Veränderungen in der Struktur der Pigmentierung zu bemerken. Die strukturellen Veränderungen befinden sich vor allem im Randbereich. Die Pfeile zeigen einige Stellen. Es handelt sich um eine der erwähnten **vier signifikanten Veränderungen im Long-Term Monitoring (6-12 Monate)**:
- asymmetrische Vergrösserung
- fokale (punktuelle) Veränderungen von Struktur oder Pigmentierung (**hier der Fall**)
- Anzeichen einer Regression
- Veränderung oder Neuauftreten einer Farbe

Illustration 4: Part of the tutorial, example 2 with comments (in German)



Tutorial (3): Hier handelt es sich um einen spezielleren Fall:
Man erkennt hier im Verlauf deutlich den Rückgang der Rötung (Entzündungsreaktion; *siehe gestrichelte Linie auf nächstem, vergrössertem Bild*).
Dies entspricht einer der **fünf unbedenklichen Veränderungen** in der Langzeit-Verlaufskontrolle (6-12 Monate):
- Aufhellung oder Dunklerwerden des ganzen Muttermales
- Veränderung in der Zahl oder der Verteilung "brauner Kügelchen"
- Rückgang in der Anzahl "schwarzer Punkte"
- Verschwinden einer Entzündungsreaktion (Rötung) (**hier der Fall**)
- Verschwinden von Teilen des Muttermals aus der Mitte und Ersatz durch hellbraune Pigmentierung

Wenn man ganz genau hinschaut, ist auch der Punkt „Veränderung in der Zahl oder Verteilung braunen Kügelchen" erfüllt, v.a. im unteren Teil des Muttermals *(siehe oval auf nächstem, vergrössertem Bild)*.

Illustration 5: Part of the tutorial, example 3 with comments (in German)

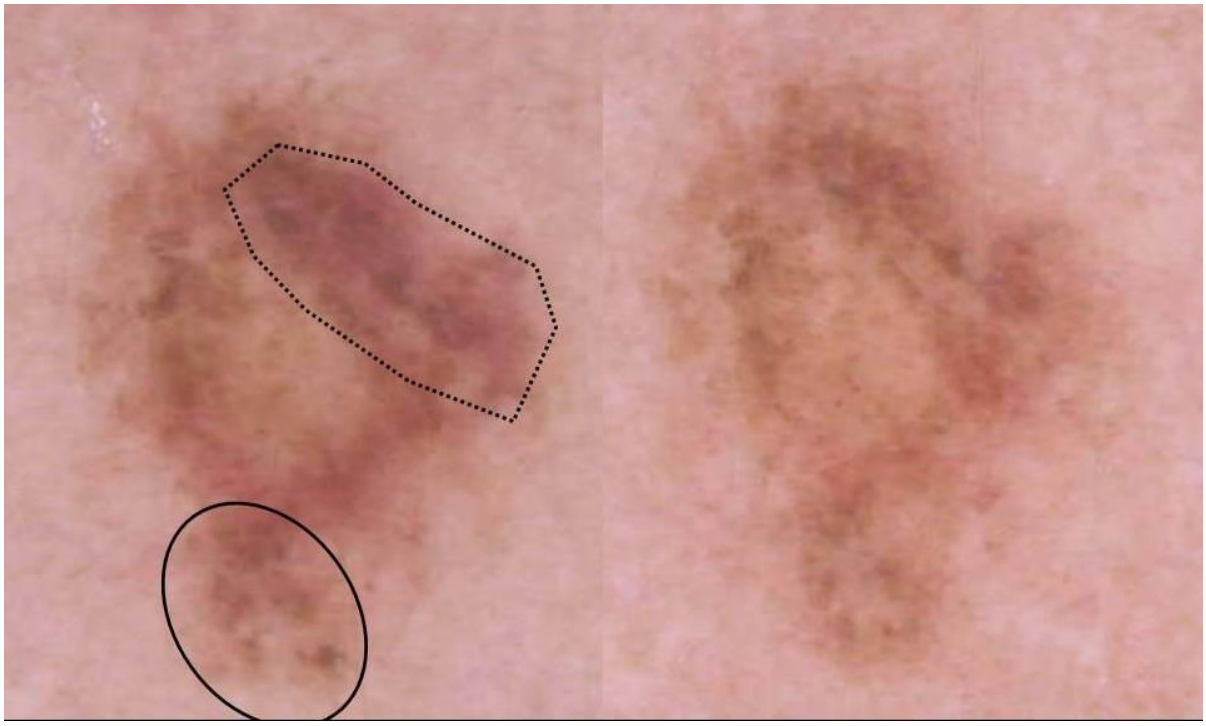
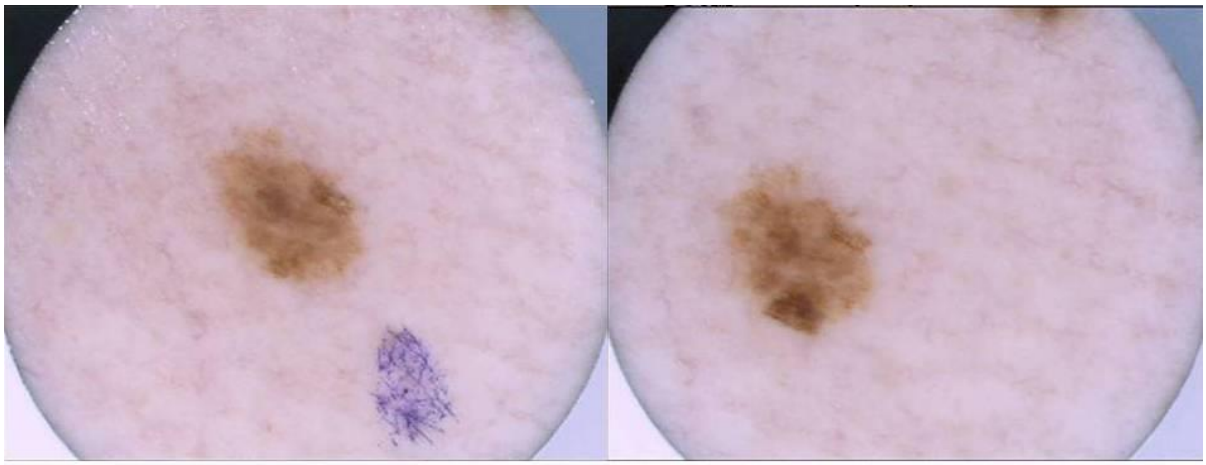


Illustration 6: Part of the tutorial, magnification of example 3



Tutorial (4): Im Verlauf (Follow-Up, rechts) sind gleich **zwei bedenkliche Veränderungen** der Langzeit-Verlaufskontrolle (6-12 Monate) zu erkennen:
1. Die Grösse hat **asymmetrisch**, d.h. nicht in alle Richtungen gleich ausgeprägt, **zugenommen** (*siehe Pfeile auf dem nächsten, vergrösserten Bild*).
2. **Fokale Veränderungen der Pigmentation** sind zu erkennen, eine ganz prominent am unteren Rand *(siehe Kreis auf dem nächsten, vergrösserten Bild)*.

Illustration 7: Part of the tutorial, example 4 with comments (in German)

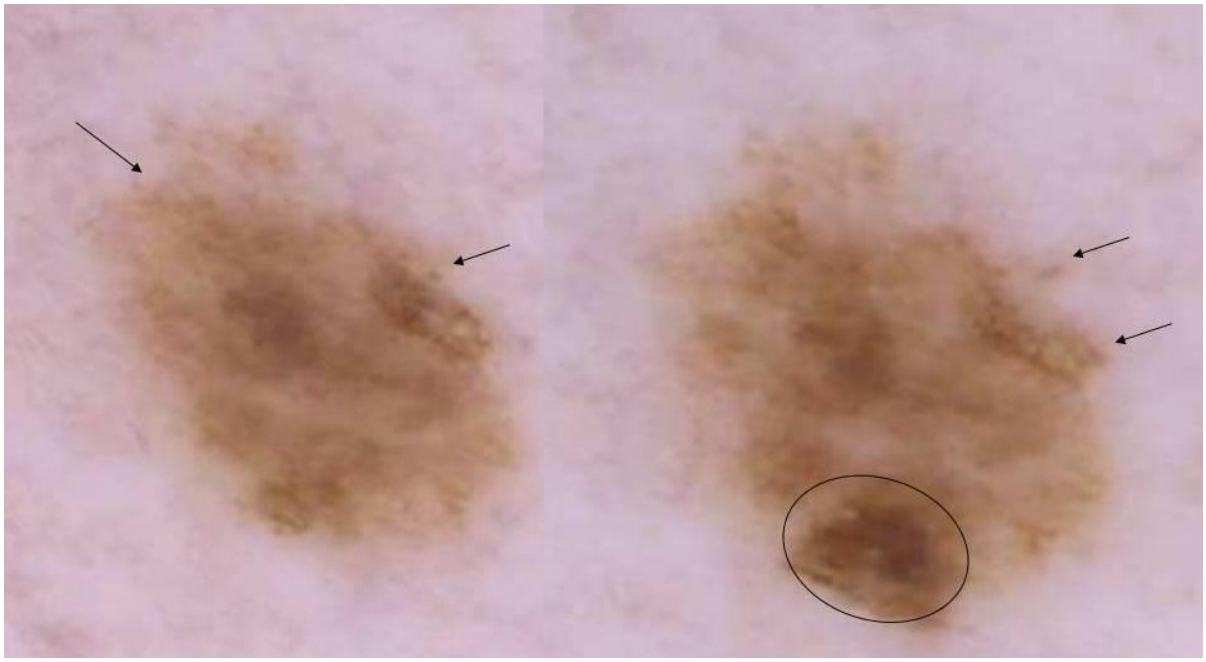


Illustration 8: Part of the tutorial, magnification of example 4

4.3. Participants

The participants of the survey which provided data for the data collection part of this paper were recruited on a completely voluntary basis. In a first attempt, patients of the mole consultation at the University Hospital of Zurich were informed about the existence of the project. This happened in an oral way during or mainly after a consultation or via a flyer which was distributed and displayed in the waiting room (see attachment). Furthermore, in the context of an information event for patients on the subject of skin cancer in general, the possibility of an anonymous participation was mentioned and encouraged. Whether a patient got the link for the feedback or the no feedback version of the survey was completely random. The only exclusion criterion was non-understanding of German language. In a second round, dermatologists, future dermatologists and medical students doing an internship in dermatology ("Unterassistenten") got access to the survey in a separate collector. The link was sent in an internal email to the medical personnel of the dermatology department of the University Hospital Zurich. They went through a feedback version of the survey in order to have a maximum of educational effect for the many younger colleagues.

4.4. Definitions

The primary endpoint of the study part of the paper was to find out if patients were able to assess whether or not a lesion in short- or long-term monitoring has changed significantly when comparing follow-up and baseline pictures of the same lesion after a short tutorial on how to do so. Significance of this endpoint was previously defined as more than 90 % concordance with the assessment by an expert dermatologist (Prof. Dr. med. Scott W. Menzies), seen over all observations. In the best case, each participant who completed the survey contributed 30 observations since the main survey part consisted of 30 cases.

Additional secondary endpoints were the difference of concordance between the group with feedback after every assessment and the other group without feedback as well as the difference of concordance between the overall concordance of patients and in contrast to the participants with dermatological background.

Moreover, the attitude of the participants towards the aspect of self-monitoring was of peculiar interest.

4.5. Statistics

Before starting the survey, some careful statistical considerations regarding sample size and power estimation have been made. The data set was determined to contain 30 observations. The proportion of change in the dataset was defined to be 20 % (or 6 out of 30 cases). Thus, the only parameter about to change was considered the number of enrolled participants or the number of observations respectively since not every participant assessed all 30 cases. It was considered a paired agreement study with a dichotomous outcome for both the gold standard (0 = no change, 1 = change) and the change variable for the evaluations of the participants (0 = no change, 1 = change). To calculate a proportion of overall concordance, the 0/0 and 1/1 observations were added.

For the following analysis of data, SurveyMonkey (SurveyMonkey Inc., San Mateo, California, USA), Excel (Version 2010; Microsoft Cooperation, Redmond, Washington, USA) and SPSS (IBM SPSS Statistics for Windows, Version 22.0; IBM Corp, Armonk, New York, USA) were used for descriptive statistics and t-test for the comparison of the different subgroups.

4.6. Ethics

We exclusively used dermoscopic (close up) images of individual lesions from a research database at the Sydney Melanoma Diagnostic Centre. The Australian patients remain completely anonymous as only the skin lesions are visible in the images without any hints of the personality, not even disclosing the exact anatomic site of the lesion. Moreover, these patients had given their consent that the images could be used for the purpose of research later on. The usage of their provided images had no influence on the patients' treatment since they were chosen retrospectively and therapeutic management had already been decided. Neither had the project any influence on the treatment of the participants completing the survey.

At the beginning of the survey, the participants were asked to fill in some demographic and statistical information about themselves such as sex, approximate age or the information whether they had ever shown a mole to a doctor or had had one excised before. Nevertheless, the reply to all these questions was voluntary and no further information about their personality or identity was inquired. Participants could always proceed to the next question without answering.

Considering the fact that both the patient whose image is part of the mole database and thereby of this study and the actual participant of the study remain completely anonymous, we applied for a waiver from the cantonal ethics commission (Gesuch BASEC-Nr. Req-2016-00415) which we received on 25 July 2016. Thereby it was stated that the project will be conducted in compliance with the Declaration of Helsinki.

5. Current Points of View and Development in Diagnostics

Melanoma detection still remains difficult. Considering the mentioned continuously increasing incidence rates,[1] every endeavour has to be made in order to decrease mortality and morbidity. The focus thereby lies on secondary prevention, on a better early detection. Various technologies more advanced than the common handheld magnifiers are under development and some of them have already been tested in clinical trials with interesting results.[16, 17] Nevertheless, for a new technology such as a new imaging device to be established, more than a few conditions have to be fulfilled. Individuals with multiple lesions are particularly in the need of good approaches in the frame of an accurate routine control of their skin. Building on the global technology development in general, there are also methods that aim at involving patients in the process of melanoma diagnosis.

This chapter gives a short overview of current points of view and development in diagnostics of melanoma.

5.1. Already Established: Sequential Digital Dermoscopy Imaging („Monitoring“; SDDI)

Dermoscopy is a form of surface microscopy. Thanks to incident non-polarised light rays, a magnifier and immersion oil between the skin and the microscope, it is possible to examine cutaneous lesions and to say whether or not they are melanocytic.[18] The immersion oil makes the epidermis layers more translucent by reducing their reflection. With behalf of a handheld magnifier (normally a magnification of x 10 is used) this allows a detailed examination of the epidermis, the following dermo-epidermal junction and to a lesser extent the underlying upper papillary part of the dermis and its pigmented structures.[18] This technique enables the examiner to discriminate morphological features which are not visible to the naked eye. Hence, dermoscopy contributes to a better diagnosis of not only melanoma but nearly all pigmented lesions.[18] At the same time, the number of unnecessary biopsies and thereby the burden of morbidity can be lowered.[12, 16] Dermoscopy has been used by many dermatologists for the last two decades and constitutes a meanwhile established element in melanoma diagnosis. Further progress in technology and digital imaging equipment made it possible to store dermoscopic images. At a later point,

the images can easily be retrieved and compared to an earlier picture.[12] This is what is called “monitoring”. Sequentially taken images of the same skin lesion are compared in order to assess whether or not a lesion has undergone any significant change. With the aid of dermoscopy and the necessary imaging and storing software, an assessment of changes in subsurface structures is possible which could not be visualized by conventional photography.[12]

There are two settings in which digital surface microscopic monitoring is frequently found: Long-term monitoring and short-term monitoring.[9, 13] Long-term monitoring is indicated when atypical nevi have to be monitored in context of regular skin examination.[13] Often patients with multiple doubtful melanocytic lesions are concerned as they have an increased risk of developing melanoma.[12] The thereby monitored lesions have usually been classified as nonmelanoma lesions before but are still monitored in order to detect possibly emerging early melanomas as soon as possible.[12, 13]

Short-time monitoring on the other hand is not specially reserved for patients with multiple nevi but for any individual lesion remaining doubtful without satisfying the dermoscopic criteria of melanoma[9] (surface microscopic features of invasive melanoma according to Menzies et. al[18, 19] in the attachment). The appropriate time interval for short-time monitoring has been assessed in different studies with the conclusion in 2008 that a period of three months remains the standard for ST-SDDI not leading to an increased risk for the patient.[13, 20] For the LT-SDDI, a follow-up period of 6-12 months on average is usual, this often happens in the context of life-long regular skin examinations.[12] The purpose of this form of mole monitoring is to discover it early enough in case a lesion shows change indicating malignancy. Kittler and Menzies 2005 contributing to the atlas of dermoscopy defined the forms of change and classified them into significant and non-significant (see table 1 below, see illustrations 3-8 in subchapter 4.2).

Table 1: Classification of changes[12]

Change	***Short-term mole monitoring (3 months)***	***Long-term mole monitoring (6-12 months)***
Significant	Any other change other than the two non-significant changes	- Asymmetric enlargement - Focal changes in pigmentation or structure - Regression features - Change in colour
Non-significant	- Global change in pigmentation (for instance solar-induced) - Loss or appearance of milia-like cysts	- Darker or lighter overall appearance - Change in number or distribution of brown globules - Decrease in number of black dots - Disappearance of inflammatory reaction - Disappearance of small foci of pigment network within central portion of the lesion and replacement by diffuse brown pigmentation

When it comes to short-term monitoring, any other change than two non-significant changes are considered worrying. Both increase or decrease in the number of small white milia-like cysts in the lesion and an overall change in pigmentation of the lesion were determined as non-significant. The latter change is often solar-induced and affects the surrounding skin as well as the lesion itself. Lesions which underwent other changes during short-term monitoring require an excision after the monitoring period.[12]

Participants of the survey for the data collection part of this study were taught exactly this classification in the tutorial.

However, dermoscopy does not bear a sensitivity of 100 % in melanoma detection either and its successful employment increases with training and growing experience of the user.[12, 16] Nevertheless, dermoscopy enhances early detection of melanoma and reduces the number of unnecessary biopsies and has therefore become an indispensable tool.[16]

Since there is still a considerable amount of melanomas which totally lack specific surface microscopic features, dermoscopy is not supposed to be used as sole indicator for excision. Based on the fact that change is a sensitive marker, monitoring becomes utterly important adding the time factor as an additional diagnostic criterion.[13, 18, 21] Especially incipient melanoma still lacking classic features can be detected.[22]

The fact that not even the most trained dermoscopist would reach 100 % sensitivity in melanoma detection underlines the necessity of additional equipment for professionals. In contrast, the principles of dermoscopy or particularly of dermoscopic monitoring are about to be taken to another level, a level gradually accessible to the patient. This is going to be addressed in the following two subchapters.

5.2. Emerging Approaches for Professionals

Various imaging devices have come onto the market during the last few years based on different technical approaches. They are about to be addressed and investigated in studies and presented and demonstrated to dermatologists and primary care physicians (PCPs) on congresses, such as in Zurich in September 2016 and 2017. This seems necessary because specialists and PCPs are not yet completely familiar with all these new possibilities and aids in skin examination.

Building on the established principle of dermoscopy, the German company FotoFinder (Bad Birnbach, Germany) shaped what is also called “Total body imaging”. It developed a system called “Automated Total Body Mapping” (ATBM®). For the first time, a camera automatically takes images of the entire patient, from their head to their toes. In the course of this, an integrated laser system along with a so-called “Ghost Feature” guarantees that patients are standing in reproducible positions while these photographs are taken.[23] This system takes dermoscopic images which are rapidly assembled to total body photos, or in other words “total body maps”. These mole maps are saved. On the one hand, the system provides a monitoring of many existing lesions simultaneously by comparing the images automatically to prior ones that were stored, on the other hand, it detects newly emerging nevi. FotoFinder emphasises in its brochure that many melanomas develop de novo and not from lesions that existed before.[23] Moreover, a software function called Moleanalyzer provides a second opinion by calculating a malignancy score for suspicious pigmented

lesions.[23] Total body imaging seems to be beneficial particularly for patients with a lot of lesions or too many lesions to track otherwise.[4, 17] Compared to manual photography of the whole body, the FotoFinder system is time saving. So far, studies are controversial when it comes to changes of the biopsy rates thanks to total body imaging.[16] One study found out that total body imaging becomes most useful in patients older than 50 years where 30 % of new lesions turned out to be melanomas on biopsy compared to 1 % in the individuals younger than 50 years.[16] Besides dermoscopy, total body imaging or mole mapping is becoming more commonplace and is one of the most frequently used tools in non-invasive diagnosis of melanoma.[17] If the use of these two important techniques is combined, limitations of their singular use are optimized.[4] Recently, total body imaging witnessed an evolution towards 3D representation of the patient in form of an avatar by combining the so far established total body imaging with SDDI which is considered to have a great potential and likely to fulfil the criteria of a good imaging system.[4]

A further tool that has moved into focus is reflectance confocal microscopy (RCM). This technique provides a resolution of the skin tissue which can be compared to conventional histopathology.[24] As the name already reveals, its mechanism is based on reflectance. Backscattering from an outgoing near-infrared laser (830 nm) is detected emanating only from the in focus plane.[24, 25] It is captured by the microscope and horizontal black-white images with a high resolution are produced.[24, 25] Highly reflective components of the skin such as melanin, collagen and keratin appear bright due to their high refractive indices.[25] The skin can be visualised as far down as the papillary dermis in depth and cytological atypia as well as displacements in architecture become depictable. For the diagnosis of melanoma and its different subtypes, criteria have been worked out and tested for diagnostic accuracy.[24] Amongst them, the presence of “pagetoid spread” is one of the most prominent criteria.[24] An established company in the field of RCM is MAVIG GmbH (Munich, Germany). With the development of their handheld VivaScope 3000, even challenging skin areas for instance in the face can be visualised. In a systematic review Edwards et al. 2017 concluded that the use of VivaScope subsequent to dermoscopy may improve the diagnostic accuracy of skin lesions compared to the use of dermoscopy alone, particularly for melanoma.[26] They refer to a study where both sensitivity and specificity of melanoma diagnosis were significantly higher for the combined use of dermoscopy and VivaScope compared with dermoscopy alone. Furthermore, they mention other

possible applications of VivaScope, for instance as a guide to surgery for better margin delineation and more complete excisions for lentigo maligna or in diagnosis of BCC and SCC.[26] Longo et al. 2012 referred to RCM as “in vivo dermatopathology” providing a near-histologic resolution directly at the patient’s bedside within a reasonable period of time. Nevertheless, its interpretation requires histopathological understanding.[24]

One last as well non-invasive tool to be addressed in this paper is electrical impedance spectroscopy (EIS). It has been found to provide assistance in diagnosing melanoma.[16] An impedance spectrometer measures the opposition to the flow of alternating currents of various frequencies.[16, 27] The system has already proven to be able to distinguish between different stages of breast cancer cell lines.[16] The underlying idea is that cancer cells have different electrochemical properties than healthy cells and tissues.[16] After the scanning of uninvolved surrounding tissue in order to get a baseline in context of a calibration, changes in cell shape, size and membrane composition can be discovered.[27] Afterwards, an algorithm classifies the examined lesion based on the data captured from both the lesion and the surrounding skin.[27] Besides the measuring on the surrounding skin before every evaluation, the lesion has to be soaked with saline solution for 60 seconds to enhance the contact between the skin and the electrodes.[16] This makes the technique time-consuming.[16] An emerging EIS-based system is Nevisense (SciBase AB, Stockholm, Sweden). 2014, the results of the largest international prospective study of its kind in melanoma detection were published.[28] The study wanted to assess safety and effectiveness of the Nevisense system. The results show a sensitivity in melanoma detection of 96.6 % and a sensitivity of even 100 % in detection of NMSC. The specificity in melanoma detection is indicated as 34.4 %.[28] The authors stress that the Nevisense system is supposed to be used in moments when a clinician considers biopsy in consequence of clinical features or patient history. It is not meant to confirm a clinical diagnosis of melanoma. Finally, the authors conclude that Nevisense proved to be an accurate and safe device and recommend it to be used in conjunction with the clinical assessment for the risk of a lesion.[28]

In a study by Rocha et al. published in 2017, the impact of an EIS system in short-term digital dermoscopy imaging of melanocytic lesions was examined.[29] A predetermined protocol was used defining the further procedure after all the included lesions had undergone examination with Nevisense and had received an EIS-score.

EIS scores of 7-10 were excised immediately, whereas scores of 0-3 as well as 4-6 had the standard ST-SDDI over a period of 3 months.[29] Scores of 4-6 were excised in case any change appeared after 3 months, scores of 0-3 indicating a benign lesion that would not even have required SDDI. Amongst these scores no melanoma was found. Respecting this protocol, the results of the study show a sensitivity in melanoma detection of 100 %. At the same time, the addition of the use of Nevisense reduced the need for SDDI by 46.9 %.[29]

A study concerning the subject of automated classification in skin cancer detection which attracted great attention in 2017 should not go unmentioned.[30] Esteva et al. tested the performance of a single convolutional neural network using a dataset of 129'450 clinical images against the performance of 21 board-certified dermatologists.[30] They demonstrated that a form of artificial intelligence is able to classify skin cancer with a level of competence similar to certified dermatologists.[30] While the dermatologists normally make their diagnosis including contextual factors beyond visual and dermoscopic inspection, this study's system bases on a huge amount of data, even being able to classify many different visual conditions.[30] The authors see substantial benefits for the field of primary care practice but also a possible augmentation in clinical decision-making by expert dermatologists.[30]

5.3. Approaches for Patients: Devices for Smartphones and Applications

While many of the available products such as dermoscopes for smartphones like HandyScope (FotoFinder, Bad Birnbach, Germany) remain rather expensive in purchase for many patients, almost uncountable applications for smartphones have been developed lately that are much more affordable or even for free. These various applications use different tools to provide their services. The aim of the addressed tools is often to provide information or education as well as to aid patients cataloguing and monitoring suspicious lesions. Some of them as well give feedback concerning malignancy.

This project intends to investigate if patients are able to detect relevant change in monitored lesions on their own after being taught what to pay attention to. In practise, this would require a device taking pictures of sufficient quality and a software application able to store them which is necessary for observation and comparison in the context of the monitoring of a lesion. In contrast, many of the emerging applications

go further than helping the patients tracking lesions: They provide the nonclinical users with feedback concerning the likelihood of malignancy.[31] Wolf et al. 2013 evaluated in a much-noticed study four applications without identifying them.[31] Three of them used automated algorithms for their feedback. The fourth one sent all the pictures to a board-certified dermatologist for an evaluation corresponding to a form of what is called “teledermatology”.[31] In the study of Wolf et al., this last application involving teledermatology reached the highest sensitivity.[31] The authors concluded that the accuracy of the evaluated smartphone applications for melanoma diagnosis was insufficient because 30 % or more of melanomas were classified as unconcerning.[31] They even emphasised that these applications thereby hold the potential to harm users.[31]

Maier et al. 2015 evaluated an application using an algorithm based on the fractal theory in comparison to clinical diagnosis and the histopathological result.[32] With the aid of fractal analysis methods, irregular shapes and patterns can be described and quantified.[32] Since the fractal pattern of normal skin and of a lesion differs, this approach has been found a method to determine the outgoing risk of a lesion. In the study, the application reached a sensitivity of 73 % and a specificity of 83 %. Nevertheless, the scores reached by two independent dermatologists were higher, which is in accordance with the results of the study of Wolf et al. in 2013.[31, 32] The authors attest some potential to the tool in the future but emphasize at the same time that it is to date insufficient to detect melanoma accurately.[32]

Although the use of these smartphone applications has been discussed controversially amongst dermatologists, they are already being widely used.[32] According to recent studies, around 20 % of the individuals aged younger than 50 years have used an application to diagnose a skin disease at least once.[33]

6. Results

In total, 47 patients answered the survey. 30 of them participated in the survey giving feedback in the main part, 17 of them answered the survey without feedback in the main part. In addition, 19 dermatologists, future dermatologists or medical students doing an internship in dermatology (“Unterassistenzärzte”) at the University Hospital in Zurich opened the survey that had been previously sent to them by email (called participants with “dermatological background”).

A high proportion of the participants did not assess all 30 images of the main survey. In a first round, we counted all the assessed images including the ones of participants interrupting at some point and the ones from participants completing the survey separately. In total, 471 images were assessed in the feedback group as well as over 328 images in the no feedback group. The participants with a dermatological background contributed 292 assessed images in their feedback containing survey. Results are shown in table 2.

Table 2: Results

Survey variant	**Feedback** **derm. background**	**Feedback** **patients**	**No-Feedback** **patients**	**Overall** **patients**
Test Set				
Images	10	10	10	10
Participants total *n*	19	30	17	47
Images assessed	137	230	125	355
Correct assessments	113 (= 82.48 %)	194 (= 84.35 %)	105 (= 84.00 %)	299 (= 84.23 %)
Participants completed *n*	13	22	12	34
Images assessed	130	220	120	340
Correct assessments	109 (= 83.85 %)	185 (= 84.09 %)	102 (= 85.00 %)	287 (= 84.41 %)
M / SD	8.38 (SD: 1.33)	8.41 (SD: 1.26)	8.50 (SD: 1.09)	8.44 (SD: 1.19)
Main survey				
Images	30	30	30	30
Participants total *n*	19	30	17	47
Images assessed	292	471	328	799
Correct assessments	232 (= 79.45 %)	375 (= 79.62 %)	267 (= 81.40 %)	642 (= 80.35 %)
Participants completed *n*	9	14	10	24
Images assessed	270	420	300	720
Correct assessments	216 (= 80.00 %)	335 (= 79.76 %)	244 (= 81.33 %)	579 (= 80.42 %)
M / SD	24.00 (SD: 1.32)	23.93 (SD: 2.89)	24.40 (SD:1.90)	24.13 (SD: 2.49)

M: Mean, SD: Standard Deviation, n: Number

Table 3: Sensitivity, specificity, positive and negative predictive values of subgroups

Feedback derm. background	**Change (+)**	**No change(-)**		Sensitivity (a/(a+c))	72.88 %
Change (+)	43 (a)	44 (b)	87 (a+b)	Specificity (d/(b+d))	81.12 %
No change (-)	16 (c)	189 (d)	205 (c+d)	Positive predictive value PPV (a/(a+b))	49.43 %
	59 (a+c)	233 (b+d)	292 (n)	Negative predictive value NPV (d/(c+d))	92.20 %

Feedback Patients	**Change**	**No change**		Sensitivity	73.40 %
Change	69	71	140	Specificity	81.17 %
No change	25	306	331	Positive predictive value PPV	49.29 %
	94	377	471 (n)	Negative predictive value NPV	92.45 %

No Feedback Patients	**Change**	**No change**		Sensitivity	84.85 %
Change	56	51	107	Specificity	80.53 %
No change	10	211	221	Positive predictive value PPV	52.34 %
	66	262	328 (n)	Negative predictive value NPV	95.48 %

For the determination of sensitivity, specificity and positive and negative predictive value all the assessments in the main survey were counted.

When it comes to statistic features of the patients participating collected at the very beginning of the survey, 55.56 % were female and 44.44 % were male. Regarding the age distribution, most of the patients (32.61 %) were between 40 and 49 years old, 23.91 % were between 50 and 59 years old and 21.74 % between 30 and 39 years old. Only 10.87 % each were younger than 30 years or older than 60 years. 26.67 % of the patients participating stated that they were working or used to work in any field related to medicine or health care. 95.56 % stated that they have already had a mole examined by a doctor, including a PCP. 82.22 % reported to have had at least one mole excised before.

The best result seen over all participants were 29 correctly assessed images out of 30 in the main survey. It was reached in the patients' feedback-group. The participant

was a man aged between 40 and 49 years. He already did well in the test giving the correct answer in 9 out of 10 cases. He denied having a job related in any way to the health care system. He had already shown moles to a doctor and had already had at least one lesion excised.

6.1. Concordance between Patients and Expert Dermatologist

The main aim of the data collection part of this paper was to determine the extent to which patients are able to assess whether or not a skin lesion had undergone significant change themselves. The variable to measure this extent was defined to be the overall concordance between the assessments of patients and the expert dermatologist in the main part of the survey (the preceding test set not included). Out of in total 799 assessments in the main survey, 642 (= 80.35 %) were correct. When counting only cases assessed by patients answering every question of the survey, 579 out of 720 decisions (= 80.42 %, confidence interval 76.912 – 83.922 %) were correct (M = 24.13, SD = 2.49, median = 24.00 (17.00 - 29.00)). The concordance rates between the different subgroups (feedback group, no-feedback group and participants with a dermatological background) were all at about the same level. They ranged between 79.45 % (participants with dermatological background) and 81.40 % (no-feedback group) and where all slightly higher when counting only the patients or participants who assessed every case (see table 2). The level of concordance we had previously considered significant was 90 %, this has consequently been clearly missed.

6.2. Influence of Feedback on the Concordance

Another question considered in the study design was whether or not performance varies with patients getting feedback. In the group without feedback in the main survey, the reached mean is slightly higher (M = 24.40, SD = 1.897). The difference could not be shown to be significant though ($t(22) = 0.449$, $p = .658$). The suspected improving influence of the repeating feedback after every assessment not only in the test set but also in the main part of the survey could consequently not be demonstrated.

Table 4: Comparison of the performance of different subgroups

Test	M	SD	*n*
Survey variant			
Feedback	23.9286	2.89467	14
No feedback	24.4000	1.89737	10
Sex			
Male	24.8000	2.69979	10
Female	23.6429	2.30742	14
Profession			
In or related to health care	24.8333	1.60208	6
Other profession	23.8889	2.72005	18
Prior mole excision(s)			
None	24.5000	2.12132	2
At least one	24.0909	2.56179	22

M: Mean of correct assessments in the main survey out of 30 cases, SD: Standard deviation, *n*: number of participants out of 24 participants who completed the whole survey.
The t-test for comparison of the means in two independent samples was used to evaluate significance, Levene-test assuming homogeneity of variance in all four comparisons conducted. P-values reflect two-sided significance for these tests. In the Shapiro-Wilk-Test for the normal distribution in the sample a value of .107 was calculated.

6.3. Further Comparisons of the Concordance

Relying on the few pieces of statistical information collected at the very beginning of the survey, the further comparison of the performance of different subgroups did not show significant tendencies either, the data sample being small besides (see table 4).

Although men assessed more cases correctly (M = 24.80, SD = 2.700) than women (M = 23.64, SD = 2.307), the difference was not significant in the t-test ($t(22) = -1.129$, $p = .271$).

Patients that indicated working or having worked in a profession in or related to the health care system scored more correct answers (M = 24.83, SD = 1.602) than patients with different professions. Nevertheless, this result was not significant, either ($t(22) = -0.798$, $p = .433$).

Patients who stated having already undergone at least one excision of a mole before had a lower mean (M = 24.09, SD = 2.562). This find could not be shown to be significant either ($t(22) = -0.218$, $p = .830$), pointing out that there were only 2 patients that had not had a mole excised before among the participants completing the whole survey and thus being included in this comparison.

6.4. Patients' Attitudes towards Patient Driven Monitoring

At the very end of the survey the participants were asked whether or not they could imagine at all tracking their own moles by using a comparable application. 92.86 % of the answering patients stated that they could imagine using such an application personally. When it comes to the participants with dermatological background the rate of approval rises up to 100.00 %.

Moreover, the response in the conversation with patients was mostly positive.

7. Discussion

7.1. Key Findings

When it comes to the overall concordance in assessing the images, all the subgroups (feedback, no feedback and participants with a dermatological background) were correct in around 80 % of the cases. This is below the level of 90 % which had previously been determined as a significant result. Nevertheless, we consider this a respectable outcome. The main aim of the project was to find out whether digital dermoscopy monitoring is feasible by patients themselves after an initial tutorial. This is of interest with regard to the tendencies to stronger involve patients in secondary prevention and the fact that there are applicable devices and apps (see chapter 5.3) coming onto the market. These applications somehow require these investigated competences for an effective use and to serve their purpose so far.

The patients reached results that were similar to the ones of the persons with dermatological background. Surprisingly, the patients getting no feedback at all in the main survey assessed the most images correctly, this result not being significant though. This is not at all what we expected. The slide with the correct answer coming up each time, the image of the case again and a repetition of the significant changes might have become confusing or have had a tiring effect on the participant in the end by seeming overloading. The results cast doubt on the necessity of consistent feedback. As far as feedback is concerned, it remains unanswered whether or not for instance repeated feedback at the beginning of multiple short teaching sessions or tutorials would have the initially expected improving impact.

Having a look at the predictive values, it is the negative predictive value that attracts attention: In all the subgroups rates clearly over 90 % were reached (see table 3). This means when participants could not detect a significant change of the mole, in most of the cases there actually was none. That is where we see clinical potential: Patients should not end up with a false sense of security. It is important that no suspicious lesions are wrongly rated as harmless. Clearly, the negative predictive values should still be higher and the simultaneously determined positive predictive values are very low. Moreover, it has to be borne in mind that predictive values highly depend on the prevalence. In our survey the “prevalence” of significant change might have been a bit higher than in a clinical setting.

The fact that participants with dermatological background in this survey did not better than recruited patients should not be overestimated. The survey had been sent to all the doctors including ones that had only just started their formation in dermatology or medical students in their penultimate year doing an internship. Moreover, it has to be emphasised that the dermatologist (S. W. M.) who assessed and contributed the cases is an expert dermatologist with great experience in the field of dermoscopy. For expert dermatologists with less routine in the use of dermoscopy, monitoring remains a challenge as well.

7.2. Comparison to Other Papers

We found no other project to exactly compare the study part of this paper to. Currently, there is a fast-growing amount of papers which scrutinize or extensively compare several applications or address and assess teledermatology with its pros and contras. After a first highlighting of inaccuracies of four applications designated for melanoma detection by Wolf et al. in 2013,[31] Kassianos et al. identified 39 applications available for individuals as well as PCPs in a review in 2015.[34] For the first time, they evaluated in particular the contents and functions of applications and investigated whether these apps have been scientifically validated or not. Amongst other things, they supposed that applications containing self-monitoring techniques instead of only providing information about skin cancer might be more effective when it comes to the patients' self-management.[34] This underlines the estimated significance of self-monitoring for early diagnosis, change over the time being a sensitive indicator of malignancy and of paramount importance when it comes to incipient or featureless melanoma.[11, 12, 13] Moreover, they outlined the little evidence based on clinical input or research they found and stressed the necessity of further research.[34] They recommended to give priority to an evaluation of how skin self-monitoring could help people assess their changing moles and derive the reasonable help-seeking decision. At least indirectly our paper investigated in that direction. Nevertheless, Kassianos et al. attest the apps a great potential.[34] In a very recent work from Australia published in 2018 about artificial intelligence in dermatology and its likely forthcoming availability to both clinicians and patients, Abbott and Smith also take a stand on smartphone applications.[35] They state that especially in Australia where melanoma incidence is high[2, 3, 4] and access to dermatological care at many places remote, a

diagnostic application could increase the likelihood of an earlier diagnosis or encourage the patient to seek out medical care sooner.[35] However, they also warn of side effects such as poor selection of monitored lesions, neglect of difficultly accessible skin areas or false reassurance, mentioning patients' guidance as an absolute need.[35] It should be clear to patients which applications are reliable and accurate.[35] Therefore, Abbott and Smith demand effective regulation, binding standards and the effort to remove dangerous and inaccurate products from the market even when potentially slowing innovation.[35]

7.3. Strength and Limitations

What makes this little paper different from many other papers is the fact that it draws on the inclusion of patients in the process of monitoring to evaluate its feasibility for patients themselves. Against the background of the discussed emerging applications, we consider the question of the paper justified and important when it comes to the protection of the user from false reassurance. After having been taught the knowledge in the tutorial part of the survey, patients might also be able to balance a risk assessment potentially given by an application in a more critical way.

The conduction of the project turned out to be more difficult than expected, mainly when it came to the enrolment of patients. Although many patients took flyers and initially signalised their interest and their willingness to complete the survey, the similar could not be observed in the number of answers despite considerable endeavour. Reasons could be the felt absence of a personal need to know, the subjective impression of uselessness for instance in the frame of a good confidence or relation to the doctor or a simple lack of time, bearing in mind the completion of the survey as a whole could take long. This was mentioned at its beginning and as evident in the results, there were participants interrupting the survey. We do not want to trace the modest willingness back on an adverse attitude towards self-monitoring in general or the discussed emerging applications since a clear majority of the participating patients (92.86 %) stated that they could imagine using such an application in the future when completing the survey. Consequence of the difficulties is a low number of cases and thus limited meaningfulness and significance. Nevertheless, the bespoken results can be regarded as tendencies but must be interpreted in a speculative manner.

Going back to the study design, there is potential to optimise. In the way the survey was conducted, the participants had the freedom to complete it on different devices such as computers, laptops, tablets or even smartphones, when- and wherever they felt like it. Thereby, the same conditions for instance the same viewing quality could not be provided at all. On the other hand, making the patients completing the survey on a computer screen directly on site after a consultation might have led to even fewer completions. Besides the influence of feedback, it might have been interesting as well to depict or quantify the effect of the tutorial by creating another group that directly starts completing the survey without education. Letting only participants feeling rather or very familiar with assessing cases proceed to the main survey might be a source of bias. However, most of the patients answered alike after a first pass of the test set without repeating it. Nonetheless, it is likely that there is a selection bias since patients were recruited in a specialised consultation and hence consisted of individuals already having a certain knowledge about and paying high attention to their skin. This could play a role in the explication of the relatively high concordance. The performance of completely unaffected individuals might be lower. An additional source of recruitment should have been implemented.

Moreover, what participants assessed in this survey compulsively varies from what they would see using any of the applications when it comes to magnification or illumination of images. This applies especially for applications used without any dermoscope-like attachment. The results have to be interpreted speculatively.

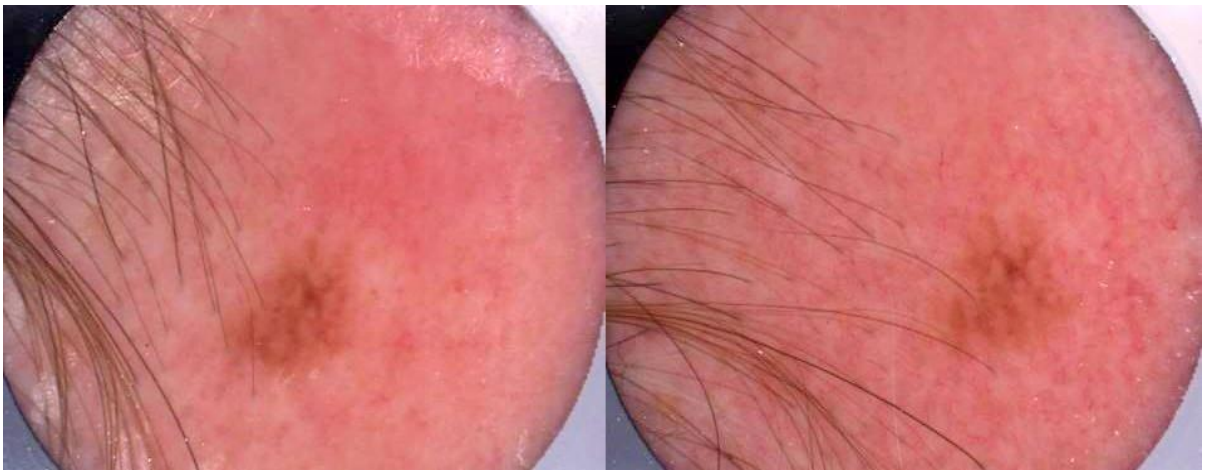


Illustration 9: Case 18/30, LT-SDDI, expert assessment: Unchanged.

Another difficulty might have been to avoid including too difficultly or too easily assessable cases in the survey. The fact that there were both cases that almost all par-

ticipants answered equally and few cases creating considerable disagreement may sustain that doubt (see illustration 9).

In the feedback variant of the survey, 53.33 % of the participants decided for significant change in this case. In the No feedback group, 72.72 % thought the lesion did not change significantly. In the group with dermatological background, there was complete discord with 50.00 % stating there was significant change and 50.00 % stating the opposite. Reasons might be the white-reddish skin type that makes it harder to identify the borders as well as the structure of pigmentation. Moreover, the lesion might have been depicted a bit twisted in the follow-up compared to baseline.

7.4. Implications of the Paper and Outlook

Although the expressiveness of the paper is minor, it has been conducted in regard of conditions which are currently in considerable motion. New technologies in melanoma diagnostics are emerging not only for professionals but also for patients. There is a kind of shift in the methods so far used by clinicians in direction of patients, for instance when it comes to the monitoring of skin lesions being of enormous significance in early diagnosis of melanoma.[12, 13] The smartphone being omnipresent among broad levels of the population is supposed to play an important role in this, for instance as a device for the self-monitoring of skin lesions.

In view of the fact that melanoma incidence is tendentially rising,[1, 2, 4] being very high for instance in Australia but also in Switzerland and causing a heavy economic burden of disease,[3, 4] there is a definite need to find good tools for the earlier detection in secondary prevention and reducing the health expenses. The dwindling resources in many health care systems make this need even more urgent. However, there are several essential criteria a suitable tool needs to fulfil. It should have a high diagnostic accuracy, save time and costs, reduce the number of unnecessary biopsies and be accessible to a wide range of population subgroups as well as PCPs.[4, 16]

The further investigation on the new applications claimed in many papers[34, 35, 36, 37] and the new tools for professionals is indispensable, as well as regulations and binding standards to ensure patients' safety and minimise harm. Abbott et Smith mention safety features included in the software such as algorithms to identify patients at high

risk and to directly guide them to appropriate care as an option.[35] Until then, caution is required and the potential benefits of skin cancer apps have to be balanced,[37] patient guidance is needed.[35] So far, patient education can only be beneficial for the use of medical applications and for self-monitoring in general and as this paper and the result of its survey indicate, education seems in a tendency feasible and favoured by many patients. In times of dwindling resources in many health care systems, patients have to accept more and more responsibility and as we show, self-monitoring might be a promising way for them to do so. For a better significance or a quantification of the impact of teaching as well as the feasibility of patient driven monitoring, similar studies should be conducted taking up our approach. They should include a higher number of patients, and patients as well as unaffected individuals. Maybe they should work with specific applications for a better comparability still using a consistent tutorial. However, it might be also interesting to compare the performance of participants being taught different tutorials for a better understanding of what the ideal tutorial for self-monitoring should look like. Another approach could be to test criteria of change other than the ones from Kittler and Menzies we used in our tutorial.[12]

Even if these applications will not turn out to be the ideal diagnostic tool longed for by many, it might have a substantial impact within the scope of escalating costs in many health care systems. There is a potential in every tool that trains for a better or more regular self-examination.[33] At the latest as far as the tutorial is concerned, it is clear that dermatologists will not be replaced, either, but need to use their skills alongside advancing technology.[35]

„No one should die of malignant melanoma“, was the title of a paper published by Ackerman in 1985[38] and as described by Rayner et al. 2018, this remains the ultimate goal of research.[35] Even though there is a long way ahead of us, the discussed new approaches and findings may shorten it if the needed further research is conducted.

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10. Curriculum Vitae

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11. Declaration

Masterarbeit

Ich erkläre ausdrücklich, dass es sich bei der von mir im Rahmen des Studiengangs

Master of Medicine (M Med) der Medizinischen Fakultät der Universität Zürich

eingereichten schriftlichen Arbeit mit dem Titel

Evaluation of Patient Driven Digital Mole Monitoring

um eine von mir selbst und ohne unerlaubte Beihilfe sowie *in eigenen Worten* verfasste Masterarbeit* handelt.

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Sanktionen

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Ich bestätige mit meiner Unterschrift die Richtigkeit dieser Angaben.

Datum: 30. Oktober 2018

Name: Marfurt Vorname: Severin

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* Falls die Masterarbeit eine Publikation enthält, bei der ich Erst- oder Koautor/-in bin, wird meine eigene Arbeitsleistung im Begleittext detailliert und strukturiert beschrieben.

12. Attachments

Attachment 1: Surface microscopic features of invasive melanoma[18, 19]

Menzies et al. 1996 worked out a method relying on 11 surface microscopic features a clinician has to be able to identify in order to diagnose invasive melanoma. They divided these features into so-called negative and positive features (see table 5).

Table 5: Menzies' Method of Diagnosis of Invasive Melanoma

Method of Diagnosis of Invasive Melanoma (Menzies et al.1996)
Negative Features (Cannot Be Found)
Point and axial symmetry of pigmentation
Presence of only one single color
Positive Features (at Least One Feature Found)
Blue-white veil
Multiple brown dots
Pseudopods
Radial streaming
Scar-like depigmentation
Peripheral black dots/globules
Multiple (5-6) colors
Multiple blue/gray dots
Broadened network

According to this model, an invasive melanoma can be diagnosed if it strictly has neither of the two negative features and at the same time at least one of the positive morphological features. This method was evaluated to provide a sensitivity of 92 % and a specificity of 71 % (Menzies et al. 1996). This result has been described as reproducible (Menzies et al. 1996).

Precise descriptions of the complete 11 morphological features can be found in:
Menzies S, Crotty K, Ingvar C, McCarthy W. An Atlas of Surface Microscopy of Pigmented Skin Lesions. Sydney, Australia: McGraw-Hill International Book Co; 1996.

Attachment 2: Example of the two-sided flyer used for the enrolment of participants

QR-Code auf der Rückseite verwenden oder
https://de.surveymonkey.com/r/muttermale2
in Webbrowser eingeben

Können Patienten ihre Muttermale selbst überwachen? Um das herauszufinden, brauchen wir Ihre Mithilfe!

Prof. Dr. med. Ralph Braun und ich führen eine Befragung durch, bei der wir sehen möchten, wie gut Veränderungen an Muttermalen über die Zeit beurteilt werden können.
—› *Weitere Informationen auf der Rückseite*

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- Die Umfrage erfolgt bis auf wenige statistische Angaben anonym.
- Sie werden eine kurze Einführung mit Tutorial erhalten und anschliessend Vorher- und Nachher-Bilder von Muttermalen bezüglich möglicher Veränderungen beurteilen.
- Sie können dabei auch für sich etwas lernen - mitmachen lohnt sich!

QR-Code verwenden oder
https://de.surveymonkey.com/r/muttermale1
in Webbrowser eingeben

Bei Fragen und Anregungen zögern Sie bitte nicht, mich zu kontaktieren:
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